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NEWS 1		Web Page URLs for STN Seminar Schedule - N. America
NEWS 2	Apr 08	"Ask CAS" for self-help around the clock
NEWS 3	Apr 09	BEILSTEIN: Reload and Implementation of a New Subject Area
NEWS 4	Apr 09	ZDB will be removed from STN
NEWS 5	Apr 19	US Patent Applications available in IFICDB, IFIPAT, and IFIUDB
NEWS 6	Apr 22	Records from IP.com available in CAPLUS, HCAPLUS, and ZCAPLUS
NEWS 7	Apr 22	BIOSIS Gene Names now available in TOXCENTER
NEWS 8	Apr 22	Federal Research in Progress (FEDRIP) now available
NEWS 9	Jun 03	New e-mail delivery for search results now available
NEWS 10	Jun 10	MEDLINE Reload
NEWS 11	Jun 10	PCTFULL has been reloaded
NEWS 12	Jul 02	FOREGE no longer contains STANDARDS file segment
NEWS 13	Jul 22	USAN to be reloaded July 28, 2002; saved answer sets no longer valid
NEWS 14	Jul 29	Enhanced polymer searching in REGISTRY
NEWS 15	Jul 30	NETFIRST to be removed from STN
NEWS 16	Aug 08	CANCERLIT reload
NEWS 17	Aug 08	PHARMAMarketLetter(PHARMAML) - new on STN
NEWS 18	Aug 08	NTIS has been reloaded and enhanced
NEWS 19	Aug 19	Aquatic Toxicity Information Retrieval (AQUIRE) now available on STN
NEWS 20	Aug 19	IFIPAT, IFICDB, and IFIUDB have been reloaded
NEWS 21	Aug 19	The MEDLINE file segment of TOXCENTER has been reloaded
NEWS 22	Aug 26	Sequence searching in REGISTRY enhanced
NEWS 23	Sep 03	JAPIO has been reloaded and enhanced
NEWS 24	Sep 16	Experimental properties added to the REGISTRY file
NEWS 25	Sep 16	CA Section Thesaurus available in CAPLUS and CA
NEWS 26	Oct 01	CASREACT Enriched with Reactions from 1907 to 1985
NEWS 27	Oct 21	EVENTLINE has been reloaded
NEWS 28	Oct 24	BEILSTEIN adds new search fields
NEWS 29	Oct 24	Nutraceuticals International (NUTRACEUT) now available on STN
NEWS 30	Oct 25	MEDLINE SDI run of October 8, 2002
NEWS 31	Nov 18	DKILIT has been renamed APOLLIT
NEWS 32	Nov 25	More calculated properties added to REGISTRY
NEWS 33	Dec 02	TIBKAT will be removed from STN
NEWS 34	Dec 04	CSA files on STN
NEWS 35	Dec 17	PCTFULL now covers WP/PCT Applications from 1978 to date
NEWS 36	Dec 17	TOXCENTER enhanced with additional content
NEWS 37	Dec 17	Adis Clinical Trials Insight now available on STN
NEWS 38	Dec 30	ISMEC no longer available
NEWS 39	Jan 13	Indexing added to some pre-1967 records in CA/CAPLUS
NEWS 40	Jan 21	NUTRACEUT offering one free connect hour in February 2003
NEWS 41	Jan 21	PHARMAML offering one free connect hour in February 2003
NEWS 42	Jan 29	Simultaneous left and right truncation added to COMPENDEX, ENERGY, INSPEC
NEWS 43	Feb 13	CANCERLIT is no longer being updated
NEWS 44	Feb 24	METADEX enhancements
NEWS 45	Feb 24	PCTGEN now available on STN

NEWS 46 Feb 24 TEMA now available on STN
NEWS 47 Feb 26 NTIS now allows simultaneous left and right truncation
NEWS 48 Feb 26 PCTFULL now contains images

NEWS EXPRESS January 6 CURRENT WINDOWS VERSION IS V6.01a,
CURRENT MACINTOSH VERSION IS V6.0b(ENG) AND V6.0Jb(JP),
AND CURRENT DISCOVER FILE IS DATED 01 OCTOBER 2002
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L1 611 ULLRICH AXEL

=> s bange johannes /au
L2 12 BANGE JOHANNES

=> s knyazev pjotr /au
L3 5 KNYAZEV PJOTR

=> s mutat? (s) fgf (s) receptor
L4 631 MUTAT? (S) FGF (S) RECEPTOR

=> s mutat? (s) fgf (s) receptor (s) transmem?
L5 51 MUTAT? (S) FGF (S) RECEPTOR (S) TRANSMEM?

=> s mutat? (s) fgf (s) receptor (s) transmem? (s) domain
L6 38 MUTAT? (S) FGF (S) RECEPTOR (S) TRANSMEM? (S) DOMAIN

=> dup rem l6
PROCESSING COMPLETED FOR L6
L7 14 DUP REM L6 (24 DUPLICATES REMOVED)

=> d l7 total ibib kwic

L7 ANSWER 1 OF 14 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 2002092821 MEDLINE
DOCUMENT NUMBER: 21633953 PubMed ID: 11772395
TITLE: The fibroblast growth factor receptor, FGFR3, forms gradients of intact and degraded protein across the growth plate of developing bovine ribs.
AUTHOR: Pandit Sujata G; Govindraj Prasanthi; Sasse Joachim; Neame Peter J; Hassell John R
CORPORATE SOURCE: The Center for Research in Skeletal Development and Pediatric Orthopedics, Shriners Hospital for Children, 12502 North Pine Drive, Tampa, FL 33612, USA.
SOURCE: BIOCHEMICAL JOURNAL, (2002 Jan 15) 361 (Pt 2) 231-41. Journal code: 2984726R. ISSN: 0264-6021.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200202
ENTRY DATE: Entered STN: 20020202
Last Updated on STN: 20020215
Entered Medline: 20020214

AB Point **mutations** in the human fibroblast growth factor (**FGF**) **receptor** 3 gene (Fgfr3) produce a constitutively active **receptor**, which disrupts chondrocyte differentiation in the growth plate and results in skeletal dysplasias with severe shortening of the limbs. Alternative splicing of the Fgfr3 transcript gives rise to two isoforms, IIIc and IIIb, which vary in their specificity for **FGF** ligands. We examined the expression of these FGFR3 isoforms in the bovine fetal rib growth plate to determine whether levels. . . the pericellular region of reserve chondrocytes and to the extracellular matrix in the hypertrophic zone. These results suggest that the **transmembrane** form of FGFR3 increasingly undergoes proteolytic cleavage towards the hypertrophic zone to produce an extracellular-**domain** fragment of FGFR3, which is present in large amounts in the matrix of hypertrophic cells. These findings suggest a proteolytic regulatory mechanism for FGFR3, whereby Fgfr3 fragments could control availability of **FGF** for the intact **receptor**, and by which proteolysis could inactivate the **receptor**.

L7 ANSWER 2 OF 14 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2001:493048 BIOSIS
DOCUMENT NUMBER: PREV200100493048
TITLE: Nuclear trafficking of FGFR1.
AUTHOR(S): Myers, J. (1); Ostrowski, J. (1); Popescu, G. (1); Stachowiak, M. K. (1)
CORPORATE SOURCE: (1) Pathology and Anatomical Sciences, SUNY at Buffalo, Buffalo, NY USA
SOURCE: Society for Neuroscience Abstracts, (2001) Vol. 27, No. 1, pp. 653. print.
Meeting Info.: 31st Annual Meeting of the Society for Neuroscience San Diego, California, USA November 10-15, 2001
ISSN: 0190-5295.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Several members of the **FGF** family lack signal peptide sequences

and are present only in trace amounts outside the cell. However these proteins contain nuclear localization signals and accumulate in the cell nucleus. Nuclei of different cells contain full-length **FGF receptor** 1 that plays a role in gene expression. FGFR1 enters the nucleus via nuclear pores by interacting with importin B. . . from the ER membrane prior to the nuclear uptake. FGFR1 was tagged with EGFP and its signal peptide (SP) and **transmembrane** (TM) **domains** were **mutated**. Localization of FGFR1-EGFP in live cells was examined by confocal microscopy. Association of FGFR1 isoforms with subcellular fractions was analyzed. . . anti-EGFP Ab. Wild type FGFR1 was detected inside and outside the nucleus. The nuclear fraction contained both non- and glycosylated **receptor**. The extranuclear FGFR1 was represented by nonglycosylated (cytosolic) and glycosylated (membrane) isoforms. FGFR1 (SP-) did not undergo glycosylation and was present in the cytosol, the nucleus, but not in the membrane. **Mutations** decreasing TM hydrophobicity accelerated nuclear accumulation of FGFR1, increased soluble and decreased hyperglycosylated FGFR1. Replacement of the FGFR1 TM with that of FGFR4 prevented **receptor** entry into the nucleus and increased membrane association. Conclusions: (1) nonglycosylated nuclear FGFR1 can be produced by translation outside the. . .

IT . . .
Systems of Organisms
ER membrane [endoplasmic reticulum membrane]; cytosol; nucleus; ribosome
IT Chemicals & Biochemicals
EGFP [enhanced green fluorescent protein]; **FGF receptor** 1 [fibroblast growth factor **receptor** 1]: glycosylation, localization, **mutation**, signal peptide **domain**, trafficking, translation, **transmembrane domains**

L7 ANSWER 3 OF 14 MEDLINE DUPLICATE 2
ACCESSION NUMBER: 2000513279 MEDLINE
DOCUMENT NUMBER: 20522289 PubMed ID: 11069376
TITLE: Fibroblast growth factor receptor-2 mutation analysis in human prostate cancer.
AUTHOR: Mehta P; Robson C N; Neal D E; Leung H Y
CORPORATE SOURCE: School of Surgical Sciences, The Medical School, University of Newcastle, Newcastle upon Tyne, UK.
SOURCE: BJU INTERNATIONAL, (2000 Oct) 86 (6) 681-5.
Journal code: 100886721. ISSN: 1464-4096.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200011
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20001130

AB OBJECTIVE: To assess whether **mutations** in the hot-spots of the fibroblast growth factor (**FGF**) **receptor**-2 gene (FGFR2, exons encoding the IIIa, IIIb, IIIc and **transmembrane domain**, TMD) are associated with the development of prostate cancer, as the IIIb variant is the specific **receptor** for FGF7/KGF, an androgen-inducible paracrine factor regulating prostatic growth. Materials and methods Single-strand conformational polymorphism-polymerase chain reaction (SSCP-PCR) and cycle-sequencing analysis were used to screen FGFR2 **mutations** in 30 patients with prostate cancer; corresponding blood samples were analysed from 11 of the patients. The human prostate cell. . . 10 foci of invasive cancer from three patients who underwent radical prostatectomy were also assessed. RESULTS: Positive controls containing FGFR2 **mutations** (Crouzon disease and Pfieffer syndrome) were confirmed by SSCP-PCR and sequencing.

Analysis of all prostate tumour samples and prostate-derived cell lines revealed no polymorphisms or **mutations** in the IIIa, IIIb, IIIc and TMD regions of FGFR2. CONCLUSION: FGFR2 **mutations** in the-**FGF** binding **domain** and the TMD are not frequent events in human prostate cancer.

L7 ANSWER 4 OF 14 MEDLINE DUPLICATE 3
ACCESSION NUMBER: 2000492186 MEDLINE
DOCUMENT NUMBER: 20311085 PubMed ID: 10854038
TITLE: NGF stimulation of erk phosphorylation is impaired by a point mutation in the transmembrane domain of trkA receptor.
AUTHOR: Monshipouri M; Jiang H; Lazarovici P
CORPORATE SOURCE: Patent and Trade Mark Office, US Department of Commerce, Washington, DC 20231, USA.
SOURCE: JOURNAL OF MOLECULAR NEUROSCIENCE, (2000 Feb-Apr) 14 (1-2) 69-76.
Journal code: 9002991. ISSN: 0895-8696.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200010
ENTRY DATE: Entered STN: 20001027
Last Updated on STN: 20001027
Entered Medline: 20001017

AB The nerve growth factor (NGF) trkA **receptor** is a **transmembrane** glycoprotein composed of a large extracellular ligand-binding region connected to the cytoplasmic tyrosine kinase region by a single **transmembrane domain** (TMD). To explore the role of TMD in the process of **receptor** activation, we substituted the hydrophobic amino-acid residue valine 432 with the charged amino-acid glutamic acid (designated V432E mutant) by utilizing in vitro site-directed mutagenesis. NIH 3T3 cells lacking endogenous NGF **receptors** were stably transfected with a pRc/CMV vector carrying either wild-type (trkA) or **mutated** (V432E) **receptors**. Stable transfectants were shown, using 125I-NGF binding and Western-blot analysis, to express the trkA recombinant **receptors**. Scatchard analysis revealed similar affinity for NGF in wild-type and V432E **receptors**. Although the level of basal trkA **receptor** tyrosine phosphorylation was higher in the mutant than in the wild-type, NGF stimulation of WT 11 and V432E transfectants resulted in a rapid increase in **receptor** tyrosine phosphorylation and of its intracellular adaptor protein SHC. In contrast to WT 11, V432E mutants showed very low levels of NGF-, and moderate levels of **FGF** -induced erks phosphorylation, respectively. Collectively, these findings suggest that a single substitution (V432E) in the trkA TMD results in a selective. . .

L7 ANSWER 5 OF 14 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1999:487211 CAPLUS
DOCUMENT NUMBER: 131:125450
TITLE: Use of inhibitors for the treatment of disorders related to RTK hyperfunction, especially cancer
INVENTOR(S): Ullrich, Axel; Bange, Johannes; Knyazev, Pjotr
PATENT ASSIGNEE(S): Max-Planck-Gesellschaft zur Foerderung der Wissenschaften E.V., Germany
SOURCE: PCT Int. Appl., 51 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9937299	A1	19990729	WO 1999-EP405	19990122
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
DE 19802377	A1	19990819	DE 1998-19802377	19980122
CA 2319121	AA	19990729	CA 1999-2319121	19990122
AU 9924239	A1	19990809	AU 1999-24239	19990122
EP 1049465	A1	20001108	EP 1999-903669	19990122
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2002518292	T2	20020625	JP 2000-528281	19990122
PRIORITY APPLN. INFO.:			DE 1998-19802377 A	19980122
			WO 1999-EP405 W	19990122

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

AB Diseases resulting from increased **receptor** tyrosine kinase (RTK) activity, esp. from overexpression and/or altered activity of RTKs, may be triggered particularly by a **mutation** of **FGF receptor** 4 (FGFR-4), esp. a point **mutation** in the **transmembrane domain** of FGFR-4 which leads to an exchange of a hydrophobic for a hydrophilic amino acid. Therefore, an inhibitor directed against FGFR-4 can be used for the treatment and/or prevention of cancer or metastasis. Differential diagnosis of cancer, or of a genetic predisposition for cancer, may be carried out by hybridization assay or PCR assay for nucleic acids coding for mutated FGFR-4, or by immunoassay for mutated FGFR-4. Thus, mutant FGFR-4 G388R was found in most breast cancer and neuroblastoma cell lines tested as well as some glioblastoma, uterine cancer, and squamous cell carcinoma cell lines; this mutation correlated well with RTK expression and with a poor long-term prognosis.

L7 ANSWER 6 OF 14 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.DUPLICATE 4

ACCESSION NUMBER: 2000:27621 BIOSIS
DOCUMENT NUMBER: PREV200000027621
TITLE: Angiopoietin-1 and its receptor Tie-2 participate in the regulation of capillary-like tubule formation and survival of endothelial cells.
AUTHOR(S): Hayes, Andrew J. (1); Huang, Wei-Qun (1); Mallah, Jamie (1); Yang, Dajun (1); Lippman, Marc E. (1); Li, Lu-Yuan (1)
CORPORATE SOURCE: (1) Lombardi Cancer Center, Georgetown University Medical Center, 3970 Reservoir Road, Washington, DC, 20007 USA
SOURCE: Microvascular Research, (Nov., 1999) Vol. 58, No. 3, pp. 224-237.
ISSN: 0026-2862.
DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Angiopoietin-1 (Ang-1) and its **receptor** Tie-2, a **transmembrane** tyrosine kinase uniquely expressed by endothelial cells, are shown by null **mutation** studies to be essential to developmental angiogenesis. The phenotypic abnormalities in these knockout animals suggest that Tie-2 signaling is necessary. . . into the collagen gel and form capillary-like tubules. The tubule-forming effect of Ang-1 is similar to the effect caused by **FGF**-2. A soluble form of the Tie-2 extracellular **domain**, in fivefold molar excess,

blocks Ang-1-induced tubule formation. Specific elimination of Tie-2 protein expression in cultured ABAE cells as a. . .

L7 ANSWER 7 OF 14 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1999:25239 CAPLUS
DOCUMENT NUMBER: 130:177680
TITLE: Effect of transmembrane and kinase domain mutations on fibroblast growth factor receptor 3 chimera signaling in PC12 cells. A model for the control of receptor tyrosine kinase activation
AUTHOR(S): Raffioni, Simona; Zhu, Ya-Zhen; Bradshaw, Ralph A.; Thompson, Leslie M.
CORPORATE SOURCE: Department of Physiology and Biophysics, College of Medicine, University of California, Irvine, CA, 92697, USA
SOURCE: Journal of Biological Chemistry (1998), 273(52), 35250-35259
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

IT Glycosylation
(biol.; **transmembrane** and kinase **domain mutations** effect on **FGF receptor** 3 chimera signaling in PC12 cells in relation to **receptor** tyrosine kinase activation control)

IT Nerve
(differentiation; **transmembrane** and kinase **domain mutations** effect on **FGF receptor** 3 chimera signaling in PC12 cells in relation to **receptor** tyrosine kinase activation control)

IT Protein motifs
(kinase **domain**; **transmembrane** and kinase **domain mutations** effect on **FGF receptor** 3 chimera signaling in PC12 cells in relation to **receptor** tyrosine kinase activation control)

IT Cell differentiation
(neuronal; **transmembrane** and kinase **domain mutations** effect on **FGF receptor** 3 chimera signaling in PC12 cells in relation to **receptor** tyrosine kinase activation control)

IT Axon
(outgrowth; **transmembrane** and kinase **domain mutations** effect on **FGF receptor** 3 chimera signaling in PC12 cells in relation to **receptor** tyrosine kinase activation control)

IT Phosphorylation, biological
(**receptor**; **transmembrane** and kinase **domain mutations** effect on **FGF receptor** 3 chimera signaling in PC12 cells in relation to **receptor** tyrosine kinase activation control)

IT Signal transduction, biological
(**transmembrane** and kinase **domain mutations** effect on **FGF receptor** 3 chimera signaling in PC12 cells in relation to **receptor** tyrosine kinase activation control)

IT Protein motifs
(**transmembrane domain**; **transmembrane** and kinase **domain mutations** effect on **FGF receptor** 3 chimera signaling in PC12 cells in relation to **receptor** tyrosine kinase activation control)

IT Fibroblast growth factor **receptors**
RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)
(type 3; **transmembrane** and kinase **domain** **mutations** effect on **FGF receptor** 3 chimera signaling in PC12 cells in relation to **receptor** tyrosine kinase activation control)

IT Platelet-derived growth factor **receptors**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(.beta., extracellular **domain**, fusion products, with **FGF receptor** 3; **transmembrane** and kinase **domain mutations** effect on **FGF** **receptor** 3 chimera signaling in PC12 cells in relation to **receptor** tyrosine kinase activation control)

IT 149146-03-2, Fibroblast growth factor **receptor** 3 tyrosine kinase
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**transmembrane** and kinase **domain mutations** effect on **FGF receptor** 3 chimera signaling in PC12 cells in relation to **receptor** tyrosine kinase activation control)

L7 ANSWER 8 OF 14 MEDLINE DUPLICATE 5
ACCESSION NUMBER: 1998226771 MEDLINE
DOCUMENT NUMBER: 98226771 PubMed ID: 9560232
TITLE: Targeted disruption of fibroblast growth factor (FGF) receptor 2 suggests a role for FGF signaling in pregastrulation mammalian development.
AUTHOR: Arman E; Haffner-Krausz R; Chen Y; Heath J K; Lonai P
CORPORATE SOURCE: Department of Molecular Genetics, The Weizmann Institute of Science, Rehovot, Israel 76100, USA.
SOURCE: PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1998 Apr 28) 95 (9) 5082-7. Journal code: 7505876. ISSN: 0027-8424.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199806
ENTRY DATE: Entered STN: 19980611
Last Updated on STN: 20000303
Entered Medline: 19980604

AB We disrupted the fibroblast growth factor (**FGF**) **receptor** 2 (FGFR2) gene by introducing a neo cassette into the IIIc ligand binding exon and by deleting a genomic DNA fragment encoding its **transmembrane domain** and part of its kinase I **domain**. A recessive embryonic lethal **mutation** was obtained. Preimplantation development was normal until the blastocyst stage. Homozygous mutant embryos died a few hours after implantation at. . . mass and raise the possibility that this activity is mediated by FGF4 signals transmitted by FGFR2. The role of early **FGF** signaling in pregastrulation development as a possible adaptation to mammalian (amniote) embryogenesis is discussed.

L7 ANSWER 9 OF 14 MEDLINE DUPLICATE 6
ACCESSION NUMBER: 97459672 MEDLINE
DOCUMENT NUMBER: 97459672 PubMed ID: 9315632
TITLE: Enhanced signaling and morphological transformation by a membrane-localized derivative of the fibroblast growth factor receptor 3 kinase domain.
AUTHOR: Webster M K; Donoghue D J
CORPORATE SOURCE: Department of Chemistry and Biochemistry and Center for Molecular Genetics, University of California, San Diego, La

Jolla 92093-0367, USA.
CONTRACT NUMBER: RO1 CA40573-11 (NCI)
T32 CA09523-12 (NCI)
SOURCE: MOLECULAR AND CELLULAR BIOLOGY, (1997 Oct) 17 (10) 5739-47.
Journal code: 8109087. ISSN: 0270-7306.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199710
ENTRY DATE: Entered STN: 19971105
Last Updated on STN: 20000303
Entered Medline: 19971023

AB Fibroblast growth factor (**FGF**) **receptors** (FGFRs) are membrane-spanning tyrosine kinase **receptors** that mediate regulatory signals for cell proliferation and differentiation in response to **FGFs**. We have previously determined that the Lys650-->Glu **mutation** in the activation loop of the kinase **domain** of FGFR3, which is responsible for the lethal skeletal dysplasia thanatophoric dyplasia type II (TDII), greatly enhances the ligand-independent kinase activity of the **receptor**. Here, we demonstrate that expression of this construct induces a c-fos promoter construct approximately 10-fold but does not lead to proliferation or morphological transformation of NIH 3T3 cells. In contrast, the isolated kinase **domain** of activated FGFR3, targeted to the plasma membrane by a myristylation signal, is able to stimulate c-fos expression by 40-fold, induce proliferation of quiescent cells, and morphologically transform fibroblasts. This result suggests that the extracellular and **transmembrane domains** of FGFRs exert a negative regulatory influence on the activity of the kinase **domain**. Targeting of the activated kinase **domain** to either the cytoplasm or the nucleus does not significantly affect biological signaling, suggesting that signals from FGFR3 resulting in mitogenesis originate exclusively from the plasma membrane. Furthermore, our novel observation that expression of a highly activated FGFR3 kinase **domain** is able to morphologically transform fibroblasts suggests that dysregulation of FGFR3 has the potential to play a role in human. . .

L7 ANSWER 10 OF 14 MEDLINE DUPLICATE 7
ACCESSION NUMBER: 97282703 MEDLINE
DOCUMENT NUMBER: 97282703 PubMed ID: 9136983
TITLE: Activation of **FGF receptors** by **mutations** in the **transmembrane domain**.
AUTHOR: Li Y; Mangasarian K; Mansukhani A; Basilico C
CORPORATE SOURCE: Department of Microbiology and Kaplan Cancer Center, New York University School of Medicine, New York, NY 10016, USA.
CONTRACT NUMBER: CA42568 (NCI)
SOURCE: ONCOGENE, (1997 Mar 27) 14 (12) 1397-406.
Journal code: 8711562. ISSN: 0950-9232.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199705
ENTRY DATE: Entered STN: 19970602
Last Updated on STN: 20000303
Entered Medline: 19970521

TI Activation of **FGF receptors** by **mutations** in the **transmembrane domain**.

L7 ANSWER 11 OF 14 MEDLINE DUPLICATE 8
ACCESSION NUMBER: 96421611 MEDLINE

DOCUMENT NUMBER: 96421611 PubMed ID: 8824259
TITLE: Divalent cations and heparin/heparan sulfate cooperate to control assembly and activity of the fibroblast growth factor receptor complex.
AUTHOR: Kan M; Wang F; To B; Gabriel J L; McKeehan W L
CORPORATE SOURCE: Center for Cancer Biology and Nutrition, Albert B. Alkek Institute of Biosciences and Technology, Department of Biochemistry and Biophysics, Texas A&M University, Houston, Texas 77030-3303, USA.
CONTRACT NUMBER: CA59971 (NCI)
DK35310 (NIDDK)
DK47039 (NIDDK)
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (1996 Oct 18) 271 (42) 26143-8.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199611
ENTRY DATE: Entered STN: 19961219
Last Updated on STN: 19961219
Entered Medline: 19961126

AB Polypeptides of the fibroblast growth factor (**FGF**) family are ubiquitous bioregulators within tissues whose activity is controlled by heparan sulfates within the pericellular matrix. **FGF** and the ectodomain of their **transmembrane** tyrosine kinase **receptors** (FGFR) exhibit heparin-binding **domains** that when juxtaposed in a **FGF** middle dotFGFR complex can accommodate a single, potentially bivalent, decameric polysaccharide chain in a ternary complex. Here we show that the interaction of heparin with **FGF** ligands is not affected by divalent cations. In contrast, the high affinity interaction (apparent Kd = 10 nM) of heparin. . . FGFR requires Ca2+ or Mg2+ at physiological concentrations. Divalent cations maintain FGFR in a heparan sulfate-dependent state in respect to **FGF** binding and an **FGF**- and heparan sulfate-dependent state in respect to autophosphorylation. A model is proposed where divalent cations and heparan sulfate cooperate to maintain FGFR in a conformation that restricts trans-phosphorylation between intracellular kinase **domains**. The restriction is overcome by **FGF** or constitutively as a common consequence of diverse **mutations** in FGFR associated with skeletal and craniofacial abnormalities.

L7 ANSWER 12 OF 14 MEDLINE DUPLICATE 9
ACCESSION NUMBER: 96394682 MEDLINE
DOCUMENT NUMBER: 96394682 PubMed ID: 8798788
TITLE: Ligand-independent activation of fibroblast growth factor receptors by point mutations in the extracellular, transmembrane, and kinase domains.
AUTHOR: Neilson K M; Friesel R
CORPORATE SOURCE: Department of Molecular Biology, Holland Laboratory, American Red Cross, Rockville, Maryland 20855, USA.
CONTRACT NUMBER: HD29561 (NICHD)
T32-HL-07698 (NHLBI)
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (1996 Oct 4) 271 (40) 25049-57.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Space Life Sciences
ENTRY MONTH: 199611
ENTRY DATE: Entered STN: 19961219
Last Updated on STN: 19961219

Entered Medline: 19961125

AB The fibroblast growth factor **receptors** (FGFRs) are a family of **receptor** protein tyrosine kinases that have been shown to mediate a variety of cellular processes including angiogenesis, wound healing, tumorigenesis, and embryonic development. Distinct FGFR **mutations** in individuals with autosomal dominant disorders of bone growth and development provide a unique opportunity to determine the function of FGFRs during embryonic development. To determine the consequences of these **mutations** on **receptor** function, we have made **mutations** in Xenopus FGFR1 (XFGFR1) and FGFR2 (XFGFR2) that correspond to several of the **mutations** identified in these dysmorphic syndromes. Analysis of mutant **receptor** proteins expressed in Xenopus oocytes indicates that all but one have elevated tyrosine kinase activity relative to their wild-type counterparts. Those **mutations** that give an unpaired cysteine residue in the extracellular **domain** result in intermolecular disulfide bond formation and covalent **receptor** dimerization. Microinjection of Xenopus embryos with RNA encoding mutant **receptors** with elevated tyrosine kinase activity results in ligand-independent induction of mesoderm in animal pole explants. Wild-type XFGFR1 and XFGFR2 do not induce mesoderm when injected at similar doses. Co-injection of RNA encoding a dominant negative **FGF receptor**, lacking the tyrosine kinase **domain**, together with RNA encoding various activated FGFRs inhibits mesoderm induction by a **receptor** activated by a **transmembrane domain mutation** or extracellular **mutations** that introduce an unpaired cysteine residue into the extracellular **domain** but does not inhibit mesoderm induction by **receptors** bearing a tyrosine kinase **domain mutation**. These results indicate that different point **mutations** may activate FGFRs by distinct mechanisms and that ligand-independent FGFR activation may be a feature in common to many skeletal. . .

L7 ANSWER 13 OF 14 MEDLINE DUPLICATE 10
ACCESSION NUMBER: 94200526 MEDLINE
DOCUMENT NUMBER: 94200526 PubMed ID: 8150217
TITLE: Evidence for both tyrosine kinase and G-protein-coupled pathways leading to starfish egg activation.
AUTHOR: Shilling F M; Carroll D J; Muslin A J; Escobedo J A; Williams L T; Jaffe L A
CORPORATE SOURCE: Department of Physiology, University of Connecticut Health Center, Farmington 06032.
CONTRACT NUMBER: F32 HD07509 (NICHD)
HD14939 (NICHD)
HL43821 (NHLBI)
SOURCE: DEVELOPMENTAL BIOLOGY, (1994 Apr) 162 (2) 590-9.
Journal code: 0372762. ISSN: 0012-1606.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199405
ENTRY DATE: Entered STN: 19940523
Last Updated on STN: 20000303
Entered Medline: 19940509

AB To investigate possible pathways leading to egg activation at fertilization, the ability of exogenously introduced tyrosine kinase and G-protein-coupled **receptors** to mimic events of fertilization was examined. Oocytes of the starfish Asterina miniata were injected with RNA for a chimeric **receptor** consisting of the extracellular **domain** of the beta form of the mouse platelet-derived growth factor (PDGF) **receptor** and the **transmembrane** /intracellular **domain** of the human fibroblast growth factor (**FGF**) **receptor**, or with RNA for the rat serotonin 1c

receptor. These oocytes were cultured for 1 to 3 days and then matured with 1-methyladenine. In response to PDGF or serotonin,. . . synthesis. Some of these artificially activated eggs cleaved, and some of the PDGF-activated eggs were observed to form larvae. A PDGF/**FGF receptor** with a point **mutation** which eliminated its ability to interact with phospholipase C-gamma did not cause fertilization-like responses. Thus components of a signaling pathway involving phospholipase C-gamma, characteristic of tyrosine kinase **receptors**, as well as components of a pathway involving a G-protein and phospholipase C-beta, characteristic of G-protein-coupled **receptors**, appear to be present in starfish eggs. Either or both could function in egg activation at fertilization.

L7 ANSWER 14 OF 14 MEDLINE DUPLICATE 11
ACCESSION NUMBER: 93206140 MEDLINE
DOCUMENT NUMBER: 93206140 PubMed ID: 8456318
TITLE: An essential heparin-binding domain in the fibroblast growth factor receptor kinase.
AUTHOR: Kan M; Wang F; Xu J; Crabb J W; Hou J; McKeehan W L
CORPORATE SOURCE: W. Alton Jones Cell Science Center, Inc. Lake Placid, NY 12946.
SOURCE: SCIENCE, (1993 Mar 26) 259 (5103) 1918-21.
Journal code: 0404511. ISSN: 0036-8075.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199304
ENTRY DATE: Entered STN: 19930507
Last Updated on STN: 20000303
Entered Medline: 19930422

AB Heparin or heparin-like heparan sulfate proteoglycans are obligatory for activity of the heparin-binding fibroblast growth factor (**FGF**) family. Heparin interacts independently of **FGF** ligand with a specific sequence (K18K) in one of the immunoglobulin-like loops in the extracellular **domain** of the **FGF receptor** tyrosine kinase **transmembrane** glycoprotein. A synthetic peptide corresponding to K18K inhibited heparin and heparin-dependent **FGF** binding to the **receptor**. K18K and an antibody to K18K were antagonists of **FGF**-stimulated cell growth. Point **mutations** of lysine residues in the K18K sequence abrogated both heparin- and ligand-binding activities of the **receptor** kinase. The results indicate that the **FGF receptor** is a ternary complex of heparan sulfate proteoglycan, tyrosine kinase **transmembrane** glycoprotein, and ligand.